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Inventors: Burczak et al.
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REMARKS

Claims 11, 12 and 16 are pending in the instant application. Claims 11, 12 and 16 have been rejected. Claim 16 has been amended. No new matter has been added and entry of the amendment is respectfully requested. Reconsideration is respectfully requested in light of the amendment and the following remarks.

I. Objection to Claims 16, 11 and 12

Claims 16 and 11-12 have been objected to because the preamble of claim 16 recites a method of monitoring progression of ovarian or testicular cancer in a patient but the limitations of the claims are not drawn to a patient who has ovarian or testicular cancer. Thus, in an earnest effort to advance the prosecution of this case and in accordance with the Examiner's suggestion, Applicants have amended section (a) of claim 16 to recite that measuring is in biological samples from **said** patient at selected times. Withdrawal of this objection is therefore respectfully requested.

II. Rejection of Claims 16, 11 and 12 under 35 U.S.C. § 103

Claims 16, 11 and 12 have been rejected under 35 U.S.C. § 103 as being unpatentable over Yamashita et al. (Clin Chim. Acta. 1994). The Examiner has acknowledged that Yamashita et al. do not teach a method of monitoring progression of ovarian or testicular

cancer, remission, or response to therapy of ovarian cancers or testicular cancer. However, the Examiner suggests that it would have been *prima facie* obvious to one of ordinary skill in the art, and one would have been motivated, at the time the invention was made to modify the assay of Yamashita et al. to monitor the progression of ovarian or testicular cancer in a patient because Yamashita et al. specifically teach that a wide variety of cancer types, all of which include carcinoma, demonstrate elevation of PLA2 in serum compared to normal control and it would be expected that at least a subset of ovarian and testicular cancers, carcinomas, would also present with elevation of PLA2 in serum compared to normal controls.

Applicants respectfully traverse this rejection.

MPEP § 2143 is clear; to establish a *prima facie* case of obviousness invention, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings to arrive at the claimed invention. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. The cited prior art reference, Yamashita et al.

does not meet all of these limitations.

In particular, Yamashita et al. provides no reasonable expectation of success that progression of ovarian or testicular cancer in a patient can be monitored by measuring PLA_2 levels in biological samples obtained from the patient at selected times. The Examiner relies upon Figure 1 at page 94 of Yamashita et al. in support of the Examiner's suggestion that "overexpression of PLA2 compared to normal control in serum were found in every single one of the eight cancer types tested." However, close examination of the data in this Figure shows that serum PLA2 levels in the majority of lung cancer, gastric cancer, and colorectal cancer patients examined were actually below the upper normal limit of M-PLA2 levels. Thus, while there are isolated instances of overexpression of serum M-PLA2 levels in each tissue examined, contrary to the Examiner's suggestion, such varying data between these different carcinomas is not predictive nor suggestive of serum M-PLA2 levels being useful in monitoring other types of cancer such as ovarian or testicular cancer.

Also highly variable in Yamashita et al. were results for production of M-PLA2 in various carcinoma cells lines. As discussed at page 97 of Yamashita et al., only six of sixteen carcinoma cell lines examined secreted M-PLA2 into the supernatant.

Further, this secretion varied between carcinoma cell lines of the same tissue type. For example, as shown in Table 2, 3 out of 9 gastric carcinoma cells lines had detectable levels of M-PLA2 in the supernatant while PLA2 was not detectable in the other 6. Accordingly, no general conclusions regarding the role of M-PLA2 in carcinomas can be derived by one skilled in the art from such data.

Therefore, the reference of Yamashita et al. provides no reasonable expectation of success with respect to the instant invention relating to monitoring cancer types not specifically taught by Yamashita et al.

Further, as acknowledged by the Examiner, Yamashita et al. does not teach a method of monitoring progression of ovarian or testicular cancer, remission, or response to therapy of ovarian cancers or testicular cancer. The variability of M-PLA2 serum levels in various carcinomas taught by Yamashita et al. is also not suggestive of monitoring progression of other types of cancer than those exemplified in Yamashita et al. Thus, this reference also fails to teach or suggest all the limitations of the claims.

Applicants would also like to clarify for the record that the Examiner's statement at page 3 of the Office Action regarding Yamashita et al. teaching "monitoring response to therapy in patients with cancer in liver, esophagus, colon, pancreas and

stomach cancer by ELISA assay of PLA2 expression . . ." is incorrect. The only PLA2 assay taught in Yamashita et al. is a radioimmunoassay. No ELISA assay for PLA2 expression nor results from an ELISA assay for PLA2 are disclosed in Yamashita et al.

Since Yamashita et al. fails to meet all three criteria required to establish a *prima facie* case of obviousness, withdrawal of this rejection under 35 U.S.C. § 103 is respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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